Message

From: Leahy, John [Leahy.John@epa.gov]
Sent: 2/22/2017 9:54:23 PM
To: Milewski, Elizabeth [Milewski.Elizabeth@epa.gov]; Wozniak, Chris [wozniak.chris@epa.gov]; Kough, John [Kough.John@epa.gov]; Borges, Shannon [Borges.Shannon@epa.gov]; Tapken, Wiebke [Tapken.Wiebke@epa.gov]; Nesci, Kimberly [Nesci.Kimberly@epa.gov]; Pease, Anita [Pease.Anita@epa.gov]
CC: Mendelsohn, Mike [Mendelsohn.Mike@epa.gov]; Wyatt, TJ [Wyatt.Tj@epa.gov]
Subject: RE: Oxitec OX513A

Me too

From: Milewski, Elizabeth
Sent: Wednesday, February 22, 2017 3:00 PM
To: Wozniak, Chris <wozniak.chris@epa.gov>; Kough, John <Kough.John@epa.gov>; Borges, Shannon <Borges.Shannon@epa.gov>; Tapken, Wiebke <Tapken.Wiebke@epa.gov>; Nesci, Kimberly <Nesci.Kimberly@epa.gov>; Pease, Anita <Pease.Anita@epa.gov>
Cc: Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>; Wyatt, TJ <Wyatt.Tj@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: RE: Oxitec OX513A

OK time for me.

From: Wozniak, Chris
Sent: Wednesday, February 22, 2017 2:55 PM
To: Kough, John <Kough.John@epa.gov>; Borges, Shannon <Borges.Shannon@epa.gov>; Milewski, Elizabeth <Milewski.Elizabeth@epa.gov>; Tapken, Wiebke <Tapken.Wiebke@epa.gov>; Nesci, Kimberly <Nesci.Kimberly@epa.gov>; Pease, Anita <Pease.Anita@epa.gov>
Cc: Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>; Wyatt, TJ <Wyatt.Tj@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: Oxitec OX513A

I am proposing a meeting for next Tuesday at 2pm to discuss what information we may request of Oxitec above and beyond what they have already included in their previous submissions to FDA for an INAD. While it is not yet clear whether this will take the EUP or Section 18 path moving forward, hopefully we can come up with a list of what we think is clearly necessary prior to them entering the field this spring / summer. My intuition tells me it will most likely be for an EUP submission based on clearance / timing of Guidance document #187 at FDA, but time will tell.

Please let me know if this timing will work for you and I will try to rearrange accordingly. We need to have something together by the end of next week as the proposed meeting with the company is March 6 or 7.

Thanks
Chris

https://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/ucm446529.htm Links to the EA, FONSI and related documents

From: Mendelsohn, Mike
Sent: Wednesday, February 22, 2017 12:16 PM
To: Wozniak, Chris <wozniak.chris@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Hartman, Mark <Hartman.Mark@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: Oxitec

Chris,

It looks like we will be meeting with Oxitec on March 6 or 7th. More to follow. Can you gather folks, particularly John and Shannon, as soon as possible to follow up on the issues below for human health and eco? I would also include Kimberly since she is working with EFED GS-15 biologists to discuss the fate of and non-target exposure to the mosquito products. Thanks!

1) **Discuss what info/data might be required for an Oxitec GE mosquito EUP or Section 18 risk assessment in the context of the EA done by FDA. We need to filter this through an EPA-style/FIFRA risk assessment and what additional data, if any, we need as well as how the data and information should be submitted for us to do our review.**

From: Hartman, Mark
Sent: Thursday, February 16, 2017 2:39 PM
To: Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>; Milewski, Elizabeth <Milewski.Elizabeth@epa.gov>; Tapken, Wiebke <Tapken.Wiebke@epa.gov>; Borges, Shannon <Borges.Shannon@epa.gov>; Wozniak, Chris <wozniak.chris@epa.gov>; Kough, John <Kough.John@epa.gov>; Eiden, Catherine <Eiden.Catherine@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Leahy, John <Leahy.John@epa.gov>
Subject: Eco Assessment for Genetically Modified Mosquitoes

I perused parts of the EA and there appear to be two studies that were conducted with Oxitec mosquitoes on non-target organisms. One was a predatory mosquito that was fed larvae of "modified" and control aegypti and no effects were observed. The second was a guppy feeding study using apparently eggs, larvae and adults which also did not identify a LOEC. Here is the link to the document. http://www.fda.gov/downloads/AnimalVeterinary/DevelopmentApprovalProcess/GeneticEngineering/GeneticallyEngineeredAnimals/UCM514698.pdf. Summaries of the studies are on pages 87-88.

My basic question are along these lines:

1. If we apply the biochemical data requirements to this case I believe we would ask for avian oral, avian dietary, freshwater fish acute, freshwater invert acute, non-target insect, seedling emergence and veg vigor. No fate unless you move to Tier 2.
    a. I think the plant studies are nor relevant.
    b. Avian seems relevant if birds feed on mosquitoes which they do. How would we devise a feeding study? Would a feeding study using adult mosquitoes be sufficient to cover the acute oral? If not, how would we go about dosing the birds?
    c. Does the guppy study suffice to fulfill the freshwater fish requirement? It is unlikely that it followed our guidelines so are the deviations important/impact the conclusions of the study?
    d. Can aquatic inverts be exposed? If so, how would be suggest dosing for such a study? If not, what is the rationale for making that conclusion?
    e. Does the predatory mosquito study suffice to fulfill the non-target insect requirement? Would this cover dragonflies and other insects that feed on aegypti? Are there insects that feed on adults and, if

so, could the study which used larvae suffice to cover those exposures or would we want a different study? We typically ask for three non-target insect studies for introduction of naturally occurring microbial. Understanding that exposures are different, is it sensible to only ask for one for a GE organism?

f. Is it reasonable to assume that a bee study is not needed based on lack of exposure?
g. Since we know that amphibians feed on mosquitoes would we want a tox study on frogs or would we argue that the exposure would be covered by one of the other studies?

2. Are we comfortable not requiring fate data from the outset especially considering the scrutiny around introducing a novel construct into the environment? Has Oxitec done any work that might be useful to draw conclusions on fate and transport?
3. Would we need estuarine ecotox data given the areas where the mosquitoes would be released?
4. Does the fact that we don't have any mammalian tox data lead to the need for some to cover potential exposure to non-targets? Are we comfortable, if we are able to make the argument of no exposure to humans, registering this with no mammalian tox data? Many times, even when exposure is precluded for some reason, we have a 6-pack. I know this is a human health issue but I snuck it in anyway.
5. My quick read of the EA led me to believe that the eco assessment was largely based on "impacts on populations" as opposed to an EPA-style risk assessment. Are these arguments relevant to our assessment especially in light of the fact that the EA was only covering a very small area of treatment.
6. Are there any changes we would make to any ecotox study we might require given what we know about the construct outputs or are the standard set of parameters sufficient?

2) Per our discussion at the end of today's meeting, I can pull together the EFED GS-15 biologists to discuss the fate of and non-target exposure to the mosquito products (genetic material, Wolbachia microbe, and carrier mosquitoes themselves). In order to facilitate that discussion**, can you guys provide a few things ahead of time:**

- The assessment that RD used to register the pyriproxyfen mosquito dust product. (Is this the trap product? Can I get that assessment ahead of time?)
- A life-cycle chart for mosquitoes to work off of to help walk through potential exposures (like Anna described).
- A one pager or chart of sorts describing the pieces of information that FDA considered in their Eco evaluation of Oxytech, and FDA's rationale/conclusions. (Maybe a summary of the FDA assessment?) I think this could help us identify gaps between what they did vs. what we typically do, if there are any.

I think we can probably talk about ESA & getting to a no-effect finding in more detail at the same time.

Thanks,
Kimberly

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